Appeal Brief S. Bruce

6/30/03

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant:	Carlyle, et al.	Examiner:	Paul Prebilic
Serial No.:	09/014087	Group Art Unit:	3738
Filed:	January 27, 1998	Docket No.:	01610.0053-US-01
Title:	PROSTHESIS WITH ASSOCIATED GROWTH FACTORS		

CERTIFICATE UNDER 37 C.F.R. 1.8: The undersigned hereby certifies that this Transmittal Letter and the paper, as described herein, are being deposited in the United States Postal Service, as first class mail, with sufficient postage, in an envelope addressed to: Commissioner for Patents, Alexandria, VA 22313-1450 on May 23, 2003.

Iain A. McIntyre
Name

Signature

APPELLANT'S BRIEF ON APPEAL

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Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Dear Sir:

This Brief is presented in support of the Appeal filed February 25, 2003, from the final rejection of claims 1, 2, 4-11, 14, 15, and 21-29 of the above-identified application, as set forth in the Office Action mailed October 25, 2002.

A check for $320.00 to cover the required fee for filing this Brief is enclosed. An original and two copies of the Brief are enclosed herewith.

I. REAL PARTY OF INTEREST

The Real Party of Interest is St. Jude Medical, Inc., a corporation of Minnesota.

II. RELATED APPEALS AND INTERFERENCES

There are no related appeals or interferences for the above-referenced patent application.

III. STATUS OF CLAIMS

Claims 1-2, 4-11, 14, 15, and 21-29 are pending and are the subject of this Appeal (Appendix 1, Claims).

The case was originally filed with claims 1-20. In a paper issued on March 30, 1999 (Appendix 2-A), Appellants were required to elect one of 3 groups. In a response mailed April 23, 1999 (Appendix 2-B), Appellants canceled claims 16-20 (Group III) without prejudice, and elected claims 1-1, 14-15 (Group I) with traverse. Appellants argued that claims 12-13 (Group II) could be examined without significant additional effort. In an action dated July 7, 1999 (Appendix 2-C), the Examiner made the election requirement final and withdrew claims 12-13 (Group II) from consideration.

In a subsequent response mailed October 7, 1999 (Appendix 2-D), Appellants canceled claims 12-13, and added new claims 21-28. In an amendment after final mailed January 29, 2001 (Appendix 2-E), claim 29 was added. In a response to office action after an RCE was filed, mailed August 23, 2001 (Appendix 2-Q), claim 3 was canceled without prejudice. Consequently, claims 3, 12-13 and 16-20 are currently withdrawn from consideration, and claims 1-2, 4-11, 14, 15, and 21-29 are pending.

IV. STATUS OF AMENDMENTS

An initial Office Action was mailed on March 30, 1999 (Appendix 2-A). An Amendment in response to the initial Office Action was mailed on April 23, 1999 (Appendix 2-B). A second non-final Office Action was mailed on July 7, 1999 (Appendix 2-C). An Amendment in response to the second non-final Office Action was filed on October 7, 1999 (Appendix 2-D), amending claims 1, 14, and 15, and adding new claims 21-28. A Letter to the Official Draftsperson including a Petition to Accept Photographs Under 37 C.F.R. § 1.84(B) with three sets of photographs was filed on December 2, 1999 (Appendix 2-E). Then a final Office Action was mailed on January 5, 2000 (Appendix 2-F), and an Amendment in response to it was filed on March 3, 2000, under 37 C.F.R. § 1.116 (Appendix 2-G), amending claims 1 and 14. By way of Advisory Action mailed March 28, 2000, the March 3, 2000 response was not entered into the record (Appendix 2-H). A request for a Continued Prosecution

Application (CPA) was filed on April 4, 2000 (Appendix 2-I), along with a request to enter the March 3, 2-J). An Amendment in response to the non-final Office Action was filed on August 28, 2000 (Appendix 2-K), further amending claims 1 and 14. A final Office Action was mailed on November 30, 2000 (Appendix 2-L), and an Amendment After Final in response to the Office Action was filed on January 29, 2001, under 37 C.F.R. § 1.116 (Appendix 2-M), amending claims 1 and 14 and adding new claim 29. By way of Advisory Action mailed February 12, 2001, the January 29, 2001 response was not entered into the record (Appendix 2-N). A Request for Continued Examination (RCE) was filed on February 26, 2001 (Appendix 2-O), along with a request to enter the previously filed amendment. A non-final Office Action was mailed on May 24, 2001 (Appendix 2-P). An Amendment in response to the non-final Office Action was filed on August 23, 2001 (Appendix 2-Q), amending page 17, lines 13-29 of the specification and claims 1 and 29. A final Office Action was mailed on November 29, 2001 (Appendix 2-R). An Amendment After Final in response to the Office Action was filed on January 29, 2002, under 37 C.F.R. § 1.116 (Appendix 2-S), amending claims 14, 25 and 29. By way of Advisory Action mailed February 28, 2002, the January 29, 2002 response was not entered into the record (Appendix 2-T). A Request for Continued Examination (RCE) was filed on February 28, 2002 (Appendix 2-U), along with a request to enter the amendment filed on January 29, 2002. A non-final Office Action was mailed on May 10, 2002 (Appendix 2-V). A Response to the non-final Office Action was filed on August 19, 2002 (Appendix 2-W). A final Office Action was mailed on October 25, 2002 (Appendix 2-X). An Amendment After Final in response to the Office Action was filed on January 27, 2003, under 37 C.F.R. § 1.116 (Appendix 2-Y), amending claim 25. By way of Advisory Action mailed February 7, 2003, the Examiner indicated that the January 27, 2003 response would be entered into the record for purpose of appeal and that the rejection based on 35 U.S.C. § 112, first and second paragraph of 25-28 was overcome (Appendix 2-Z). A Petition for Extension of Time and Notice of Appeal were filed on February 25, 2003 (Appendix 2-AA). Consequently, the pending claims listed included the amendment to claim 25 submitted on January 27, 2003.

V. SUMMARY OF THE INVENTION

The Appellants' invention is generally directed to polypeptide growth factors and to prosthesis having components that have been modified with such polypeptide growth factor. The invention is also related to methods of making such prosthesis. Examples of preferred growth factors include vascular endothelial cells, as detailed on page 6, line 4 to line 19, and page 6, line 27 to page 7, line 3.

The growth factors can be joined with a tissue or a synthetic substrate to promote the population of the substrate with viable cells. Examples of some joining methods are described on page 3, line 22 to page 4, line 9. Details of such joining are further disclosed, for example, in Fig. 1, 2, on page 5, line 23 to page 6, line 2; on page 6 line 20 to line ; and on page 12 line14 to page 16, line 30.

Further aspects of the invention featuring a prosthesis, an article including crosslinked tissue with associated growth factors, and methods therein are described on page 4, line 10 to page 5, line 17, page 7, lines 4 to page 9, line 27.

The subject matter of claim 1 is described in embodiments throughout the specification, for example on page 4, line 10 to page 16, line 30. The prosthesis includes allograft or xenograft tissue having a polypeptide growth factor associated with it by means of a biologic adhesive, antibody-antigen associations, specific binding protein-receptor associations or e enzyme substrate associations.

Claim 2 is dependent from claim 1 and is directed to the specific binding interactions of the growth factor to the tissue, as is disclosed, for example, on page 15, line 5 to page 16, line 2. Further discussions of specific binding interactions are disclosed in the specification.

Claim 4 is dependent from claim 1 and is directed to the binding of the growth factor to tissue using a linker molecule, as is disclosed, for example, on page 15, lines 15 to 26. Further examples of the disclosure are presented throughout the specification.

Claim 5 is dependent from claim 1 and is directed to tissue comprising crosslinked tissue, as is disclosed, for example, on page 4, lines 10 to 31, page 8, lines 12-23, and Figs. 1 and 2. Further disclosure is found throughout the specification.

Claim 6 is dependent from claim 1, and is directed to tissue comprising uncrosslinked tissue, as is disclosed, for example, on page 4, lines 19-28, and page 7, lines 5 to 30. Other discussion is found throughout the specification.

Claim 7 is dependent from claim 1, and is directed to tissue comprising a porcine heart valve, as is disclosed, for example, on page 5, lines 1- to 3, page 7, lines 14 to 30, and page 20, line 22 to page 25, line 26. Other examples of the disclosure are found throughout the specification.

Claim 8 is dependent from claim 1 and is directed to tissue comprising bovine pericardial tissue, as is disclosed, for example, on page 4, lines 19-28, and page 7, lines 14 to 30. Other examples of the disclosure are found throughout the specification.

Claim 9 is dependent from claim 1 and is directed to polypeptide growth factors comprising vascular endothelial growth factors, as is disclosed for example, on page 3, lines 16 to page 6, line 19. Other examples of the disclosure are found throughout the specification.

Claim 10 is dependent from claim 9 and is directed to growth factors comprising a protein selected from a group of proteins or combination of therein, as is disclosed for example, on page 3, line 16 to page 6, line 19. Other examples of the disclosure are found throughout the specification.

Claim 11 is dependent from claim 1 and is directed to tissue comprising synthetic tissue, as is disclosed, for example, on page 3, lines 16 to 20, and page 7, line 32 to page 8, line 11. Other examples of the disclosure are found throughout the specification.

Claim 14 is directed to a prosthetic heart valve comprising a substrate with associated VEGF. It is described in embodiments throughout the specification, for example on page 3, line 16 to page 16, line 30. The association is effected by means of direct attachment, a biologic adhesive, covalent bonding using crosslinking agents, antibody-antigen associations, specific binding protein-receptor associations or enzyme-substrate associations, the polypeptide growth factors being effective to stimulate the affiliation of viable cells with said substrate.

Claim 15 is dependent from claim 14 and is directed to a prosthetic heart valve comprising a porcine heart valve, as is disclosed for example, on page 5, lines 1 to 3,

page 7, lines 14 to 30, and page 20, line 22 to page 25, line 26. Other examples of the disclosure are found throughout the specification.

Claim 21 is dependent from claim 14, and is directed to substrate comprising tissue, as is disclosed for example, on page 4, lines 10 to 31, page 8, lines 12-23, and Figs. 1 and 2. Further disclosure is found throughout the specification.

Claim 22 is dependent from claim 21 and is directed to tissue comprising uncrosslinked tissue, as is disclosed for example, on page 4, lines 19-28, and page 7, lines 5 to 30. Other discussion is found throughout the specification.

Claim 23 is dependent from claim and is directed to tissue comprising crosslinked tissue, as is disclosed, for example, on page 4, lines 10 to 31, page 8, lines 12-23, and Figs. 1 and 2. Further disclosure is found throughout the specification.

Claim 24 is dependent from claim 14 and is directed to substrate comprising a synthetic polymer, as is disclosed, for example, on page 3, lines 16 to 20, and page 7, line 32 to page 8, line 11. Other examples of the disclosure are found throughout the specification.

Claim 25 is directed to a prosthesis comprising crosslinked tissue having an exogenous polypeptide growth factor associated with it. The embodiments are disclosed throughout the specification, for example on page 3, line 16 to page 16, line 30.

Claim 26 is dependent from claim 25 and is directed to polypeptide growth factors comprising vascular endothelial growth factor, as is disclosed for example, on page 3, lines 16 to page 6, line 19. Other examples of the disclosure are found throughout the specification.

Claim 27 is dependent from claim 25 and is directed to crosslinked tissue comprising a crosslinked heart valve, as is disclosed for example, on page 4, lines 10 to 31, page 8, lines 12-23, and Figs. 1 and 2. Further disclosure is found throughout the specification.

Claim 28 is dependent from claim 25 and is directed to crosslinking involving glutaraldehyde moieties, as is disclosed for example, on page 4, line 29 to 31, and page 6, lines 12 to 23, page 14, line 23, and page 15, line 4. Further disclosure is found throughout the specification.

The subject matter of claim 29 is described in embodiments throughout the specification, for example on page 4, line 10 to page 16, line 30. The prosthesis includes allograft or xenograft tissue having a polypeptide growth factor associated with it by means of a biologic adhesive, covalent bonding using crosslinking agents comprising reactive functional groups, antibody-antigen associations, specific binding protein-receptor associations or e enzyme substrate associations.

VI. ISSUES PRESENTED FOR REVIEW

A. Whether claims 1, 2, 4-6, 9-11, 14, and 21-29 are rejected under the judicially created doctrine of obvious-type double patenting as being unpatentable over the claims of copending Application No. 09/186810.

B. Whether claims 25 and 28 are rejected under 35 U.S.C. §102(b) as being anticipated by or, alternatively, as being unpatentable under 35 U.S.C. §103(a) over Cahalan, et al. (US 5,308,641).

C. Whether claims 25 and 26 are rejected under 35 U.S.C. §102(b) as being anticipated by or, alternatively, as being unpatentable under 35 U.S.C. §103(a) over Bayne, et al. (EP 0 476 983).

D. Whether claims 1-2, 4-5, 9-11, and 29 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Bayne, et al. in view of Wadström (US 5,631,011).

E. Whether claims 6-8, 14, 15, 21-24, and 27-28 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Bayne, et al. and Wadström as applied to claims 1-5, 9-11 and 29, and further in view of Carpentier, et al. (US 4,648,881).

VII. GROUPING OF CLAIMS

For purpose of this appeal, Appellants have grouped the claims (as shown in Appendix 1) according to the grounds of rejection made in the final Office Action, as shown below:

Issue A: Claims 1, 2, 4-6, 9-11, 14, and 21-29

Issue B: Claims 25 and 28

Issue C: Claims 25 and 26

Issue D: Claims 1-2, 4-5, and 9-11

Issue E: Claim 29

Issue F: Claims 6-8, 14, 15, 21-24, and 27-28

VIII. ARGUMENT

Issue A: Judicially created doctrine of obvious-type double patenting rejection of claims 1, 2, 4-6, 9-11, 14, and 21-29

Claims 1, 2, 4-6, 9-11, 14, and 21-29 are rejected under the judicially created doctrine of obvious-type double patenting as being unpatentable over the claims of copending Application No. 09/186810.

Appellants submit that claims 1, 2, 4-6, 9-11, 14, and 21-29 of the present application are distinct and independently patentable from the claims of copending Application Number 09/186810. Claims 1, 2, 4-6, and 9-11 are directed to a prosthesis for a human patient comprising allograft or xenograft having a polypeptide growth factor associated therewith. Claims 14,and 21-29 are directed to a prosthesis heart valve comprising substrate with associated VEGF, which are independently patentable from claims 1, 3-4, 8-11, 13, 15, and 34-40 of copending Application No. 09/186,810. Additionally, Appellants will consider filing a terminal disclaimer complying with 37 CFR 3.73(b) when these claims are allowed.

Issue B: 35 U.S.C. §102(b)/103 rejection of claims 25 and 28 based on 35 U.S.C. §102(b)

Claims 25 and 28 are rejected under 35 U.S.C. §102(b) as being anticipated by or, alternatively, as being unpatentable under 35 U.S.C. §103(a) over Cahalan, et al.

(US 5,308,641) (Cahalan, et al.). The Examiner cited Cahalan, et al. as disclosing that human or animal tissue is used as the solid surface and that the biomolecule is one of the growth factors (col. 6, lines 14-16; the abstract; col. 4, lines 20-43; and col. 6, lines 8-28).

Cahalan, et al. teaches the use of an improved spacer material and a method for making it, comprising an aminated substrate, a polyalkylimine covalently attached to the aminated substrate and a crosslinking agent. See col. 3, lines 1-20. The crosslinking agent is for crosslinking the polyalkylimine to an aminated substrate. See col. 3, lines 21-34. The polyalkylimine and crosslinking agent together form the spacer used for improving the biocompatability of the substrate to enable the attachment of any biologically active compound to the substrate through the spacer. See col. 4, lines 14-19. Cahalan, et al. further stresses that the spacer material intervenes between the substrate and the biologically active compound, and sometimes, a second spacer is used. See col. 4, lines 58-60, and col. 5, lines 44-55. It also specifically teaches controlled light crosslinking of the polyalkylimine itself to prevent the biomolecule from being buried in the spacer and losing bioactivity and also light crosslinking in the interface between the polyalkylimine and the biomolecule to attach the biomolecule to the polyalkylimine. See col. 3, lines 2-20.

On the other hand, claim 25 teaches a crosslinked tissue having an exogenous polypeptide growth factor associated with it. The crosslinking agent crosslinks the tissue with the growth factor. Appellants submit that the "crosslinked tissue" of claim 25 is different from the "lightly crosslinked" polyalkylimine in Cahalan, et al. First, the term "crosslinked" is different from "partially crosslinked or lightly crosslinked". It denotes more complete crosslinking than either "partially or lightly". Second, Cahalan, et al. specifies "lightly crosslinked" for achieving its objective of "lightly crosslinking" the polyalkylimine to the substrate on the one hand, and at the same time, "lightly crosslinking" the "lightly crosslinked" polyalkylimine to the biomolecule. Otherwise, the objective of crosslinking the polyalkylimine to both the substrate and the biomolecule will either be defeated, or Cahalan, et al. will have no need to clarify crosslinked with "lightly". See col. 3, lines 2-20.

To anticipate a claim, the reference must teach every element of the claim. "A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference." *Verdegaal Bros. v. Union Oil Co. of California*, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987). "The identical invention must be shown in as complete detail as is contained in the ... claim." *Richardson v. Suzuki Motor Co.*, 9 USPQ2d 1913, 1920 (Fed. Cir. 1989). Therefore, all claim elements, and their limitations, must be found in the prior art reference to maintain a rejection based on 35 U.S.C. §102. Appellants respectfully submit that Cahalan, et al. does not teach every element of claim 25, and therefore fails to anticipate claim 25.

Dependent claim 28, dependent from independent claim 25, was also rejected under 35 U.S.C. §102(b) as being unpatentable over Cahalan, et al. While Appellants do not acquiesce with the particular rejections to claim 28, it is believed that this rejection is moot in view of the remarks made in connection with independent claim 25. Claim 28 includes all of the limitations of claim 25, and recites additional features which further distinguish it from the cited reference. Therefore, claim 28 is also in condition for allowance.

Furthermore, the Examiner asserts that "light crosslinking" is only a preferred embodiment in the Cahalan patent and that it would be obvious to proceed to fully crosslinking the polyalkylimine. Appellants respectfully disagree. As noted above, "light crosslinking" is described as an aspect of reaching the objective of linking a biomolecule to the polyalkylamine which is already lightly crosslinked to the support. See, for example, abstract, column 3, lines 13-20, column 4, lines 66 to column 5, line 3; column 7, lines 45-50 Example 5. Light crosslinking of the polyalkylimine ties up some of the polyalkylimine sites via the aldehyde functionality of the crosslinking agent, but not all of the sites, so that some imine groups are available to bond the biomolecule to the polyalkylimine.

Also, even though Cahalan, et al teaches lightly crosslinked polyalkylimines, the Cahalan patent does not teach, suggest, or motivate "crosslinked tissue". By qualifying "crosslinked" with "lightly", Calahan et al teaches away from the "crosslinked" tissue of claim 25. Thus, specifically with respect to lack of motivation, the objectives in the

Cahalan patent are completely unrelated to the modification of material properties that would generally result from crosslinking.

Three criteria must be met to establish a *prima facie* case of obviousness. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference. Second, there must be a reasonable expectation of success. Finally, the prior art reference, or combination of references, must teach or suggest all the claim limitations. MPEP § 2142. Appellants respectfully traverse the rejection since the Cahalan patent does not teach, suggest or motivate Appellants' claimed invention. The Cahalan patent does not render claim 25 obvious.

For the purpose of this appeal only, claims 25 and 28 are grouped together. Appellants do not admit that there are no patentable differences between claims 25 and 28. Claim 28 is dependent from claim 25. It includes all of the limitations of claim 25, and recites additional features which further distinguish it from Calahan, et al. While Appellants do not acquiesce with the particular rejection to claim 28, it is believed that this rejection is moot in view of the remarks made in connection with independent claim 25. Since claim 25 is patentable, claim 28 is also patentable.

In view of the above arguments, Cahalan, et al. fails to teach or motivate one to arrive at the invention of claims 25 and 28, and claims 25 and 28 are patentable over Cahalan, et al. (US 5,308,641), under 35 U.S.C. §102(b) or, alternatively, under 35 U.S.C. §103(a).

Issue C: 35 U.S.C. §102(b)/103 rejection of claims 25 and 26 based on Bayne, et al.

Claims 25 and 26 are rejected under 35 U.S.C. §102(b) as being anticipated by or, alternatively, as being unpatentable under 35 U.S.C. §103(a) over Bayne, et al. (EP 0 476 983) (Bayne, et al.). The Examiner asserts that the Bayne EP application discloses applying fibrin coating, prior to or in addition to the VEGF II coating, onto the surface of the fixed umbilical vein, since the tubular supports include fixed umbilical vein. Appellants continue to believe that this is a misunderstanding of the Bayne EP application. Appellants respectfully request reconsideration.

Bayne, et al. noted that after an adequate number of endothelial cells are grown, these cells are plated on the inside surface of the fixed umbilical vein. See page 8, lines 14-19. No mention is made of prior coating of the umbilical vein with VEGF II or a protein like fibrin. Bayne, et al. further states that "Following implantation endothelial cells... grow on the **artificial surface**. Prior coating... with proteins such as fibrin... enhance attachment of the cells to the **artificial surface**." (emphasis added) (page 8, lines 17-23). The Bayne EP application does not disclose application of a growth factor to a fixed tissue. Rather, it discloses the application of cells to the tissue.

On the other hand, claim 25 discloses a crosslinked tissue having an exogenous polypeptide growth factor associated with it. Since the Bayne EP application does not disclose every element of the claimed invention, the Bayne EP application does not anticipate claim 25. Claim 26 depends from claim 25 and therefore incorporates all the limitations of claim 25 and is also not anticipated by Bayne, et al. Appellants respectfully request the withdrawal of the rejection of claims 25 and 26 under 35 U.S.C. §102(b) as being anticipated by the Bayne EP application.

The Examiner alternatively rejected claims 25 and 26 as unpatentable under 35 U.S.C. §103(a) over the Bayne EP application. The Examiner asserts that if the tubular supports coated with VEGF II do not include umbilical vein, then it would have been obvious to use umbilical vein as the tubular support. Appellants respectfully traverse the rejection.

Bayne, et al. discloses the application of cells to the tissue. It does not teach the association of crosslinked tissue with a polypeptide growth factor, in particular with VEGF. In addition, it teaches the association of VEGF II with an **artificial surface.** See page 8, lines 20-23. When referring to a fixed umbilical vein, no mention is made of prior coating of the umbilical vein with VEGF II or a protein like fibrin, as noted before. Therefore, Bayne, et al. does not teach, suggest or motivate application of VEGF with a crosslinked tissue, which is not an artificial surface. Thus, Bayne, et al. does not render claim 25 obvious. Since claim 26 is dependent from claim 25 and incorporates all the limitations of claim 25, it is also not rendered obvious by Bayne, et al.

Since claim 26 is dependent from claim 25 and incorporates all the limitations of claim 25, it is also not rendered obvious by Bayne, et al.

Claims 25 and 26 are grouped together for purposes of this appeal. Appellants do not admit that there are no patentable differences between claims 25 and 26.

In view of the above arguments, Bayne, et al. fails to teach or motivate one to arrive at the invention of claims 25-26 and claims 25-26 are patentable over Bayne, et al. under 35 U.S.C. §102(b) or, alternatively, under 35 U.S.C. §103(a).

Issue D: 35 U.S.C. § 103(a) rejection of claims 1-2, 4-5, and 9-11 based on Bayne, et al. in view of Wadström

Claims 1-2, 4-5, and 9-11 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Bayne, et al. in view of Wadström (US 5,631,011).). The Examiner asserts that Bayne, et al. discloses a fixed tissue coated with a fibrin coating (biologic adhesive) that is applied prior to the application of a polypeptide growth factor, VEGF, and that Wadström discloses fibrin as a common biologic tissue adhesive. The Examiner asserts that it would have been obvious to use an allograft or xenograft tissue for the umbilical vein disclosed in the Bayne EP application.

Bayne, et al. does not disclose a polypeptide growth factor or protein such as fibrin associated with the umbilical vein, as discussed above. Instead, Bayne, et al. teaches the association of VEGF II with an **artificial surface.** See page 8, lines 20-23. When referring to a fixed umbilical vein, no mention is made of prior coating of the umbilical vein with VEGF II or a protein like fibrin. This deficiency is not supplied by Wadström, as it does not teach, suggest or motivate association of a polypeptide growth factor with tissue. Wadström only teaches an improved fibrin glue without a low viscosity problem and which promotes wound healing without scar formation or development of adhesions. See col. 2, line 65 to col. 3, line 47. Since Wadström is directed to an anti-adherence composition, there is no motivation to combine the teaching of Bayne, et al. with that of Wadström, and the combined teachings do not teach, suggest or motivate the association of polypeptide growth factor with tissue. Therefore, it would not be obvious to associate a polypeptide growth factor with allograft or xenograft tissue.

In addition, Wadström does not disclose the use of a biologic adhesive to associate a growth factor with a material, as it is mainly concerned with an anti-

adherence composition. Though fibrin is a polymer, it is not an adhesive. A mixture of fibrinogen and thrombin is an adhesive, which can be called a fibrin adhesive since fibrin is formed in the reaction. See col. 1, lines 17-28. Once fibrin is formed, the adhesive properties are no longer present since the fibrin protein itself is not adhesive. See also col.1, lines 17-28. Since Bayne, et al. does not teach, suggest or motivate the use of an adhesive to associate a growth factor with a substrate, the combined disclosures of Bayne, et al. and Wadström do not teach, suggest or motivate association of a polypeptide growth factor with a substrate using an adhesive, the subject matter of claim 1.

Claims 2, 4-5, and 9-11 are dependent from claim 1. While Appellants do not acquiesce with the particular rejections to these dependent claims, it is believed that these rejections are moot in view of the remarks made in connection with independent claim 1. These dependent claims include all of the limitations of the base claim and any intervening claims, and recite additional features which further distinguish these claims from the cited references. Therefore, dependent claims 2, 4-5 and 9-11 are also in condition for allowance.

Dependent claims 2, 4-5 and 9-11 are grouped together for purposes of this appeal. Appellants do not admit that there are no patentable differences amongst claims 2, 4-5 and 9-11.

In view of the above, the combined teaching of Bayne, et al. and Wadström fail to motivate one to arrive at the invention of claims 1-2, 4-5, 9-11, and 29. These claims are patentable under 35 U.S.C. § 103(a) over Bayne, et al. in view of Wadström.

Issue F: 35 U.S.C. § 103(a) rejection of claim 29 based on Bayne, et al. in view of Wadström

Claim 29 is rejected under 35 U.S.C. § 103(a) as being unpatentable over Bayne, et al. in view of Wadström (US 5,631,011).). The Examiner asserts that Bayne, et al. discloses a fixed tissue coated with a fibrin coating (biologic adhesive) that is applied prior to the application of a polypeptide growth factor, VEGF, and that Wadström discloses fibrin as a common biologic tissue adhesive. The Examiner asserts that it

would have been obvious to use an allograft or xenograft tissue for the umbilical vein disclosed in the Bayne EP application.

Bayne, et al. does not disclose a polypeptide growth factor or protein such as fibrin associated with the umbilical vein, as discussed above. Instead, Bayne, et al. teaches the association of VEGF II with an **artificial surface.** See page 8, lines 20-23. When referring to a fixed umbilical vein, no mention is made of prior coating of the umbilical vein with VEGF II or a protein like fibrin. This deficiency is not supplied by Wadström, as it does not teach, suggest or motivate association of a polypeptide growth factor with tissue. Wadström only teaches an improved fibrin glue without a low viscosity problem and which promotes wound healing without scar formation or development of adhesions. See col. 2, line 65 to col. 3, line 47. Since Wadström is directed to an anti-adherence composition, there is no motivation to combine the teaching of Bayne, et al. with that of Wadström, and the combined teachings do not teach, suggest or motivate the association of polypeptide growth factor with tissue. Therefore, it would not be obvious to associate a polypeptide growth factor with allograft or xenograft tissue.

In addition, Wadström does not disclose the use of a biologic adhesive to associate a growth factor with a material, as it is mainly concerned with an anti-adherence composition. Though fibrin is a polymer, it is not an adhesive. A mixture of fibrinogen and thrombin is an adhesive, which can be called a fibrin adhesive since fibrin is formed in the reaction. See col. 1, lines 17-28. Once fibrin is formed, the adhesive properties are no longer present since the fibrin protein itself is not adhesive. See also col.1, lines 17-28. Since Bayne, et al. does not teach, suggest or motivate the use of an adhesive to associate a growth factor with a substrate, the combined disclosures of Bayne, et al. and Wadström do not teach, suggest or motivate association of a polypeptide growth factor with a substrate using an adhesive, the subject matter of claim 29.

In view of the above, the combined teaching of Bayne, et al. and Wadström fail to motivate one to arrive at the invention of claim 29. Claim 29 is patentable under 35 U.S.C. § 103(a) over Bayne, et al. in view of Wadström.

Issue G: 35 U.S.C. § 103(a) rejection of claims 6-8, 14, 15, 21-24, and 27-28 based on Bayne, et al. and Wadström, and further in view of Carpentier, et al. (US 4,648,881).

Claims 6-8, 14, 15, 21-24, and 27-28 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Bayne, et al. and Wadström as applied to claims 1-5, 9-11 and 29, and further in view of Carpentier, et al. (US 4,648,881). The Examiner cited Carpentier, et al. for disclosing uncrosslinked and crosslinked tissue, heart valve tissue and other types of tissue. The Examiner asserted that it would have been obvious to use these materials as the substrates within the teaching of Bayne, et al. for the application contemplated by Carpentier.

Bayne, et al. does not disclose the tissue, such as fixed umbilical vein, with the growth factor or an adhesive or specific binding interactions to associate a protein with a substrate. This deficiency is not supplied either by Wadström or Carpentier, et al. As noted above, Wadström is more directed to an anti-adherence composition, and does not teach or suggest the use of a biologic adhesive for association of active biomolecules with a substrate. Carpentier, et al. discloses treatments of tissue to reduce the incidence of calcification and does not disclose the association of biologically active proteins with tissue. Thus, there would have been no motivation to combine the teachings of these references. In addition, the combined references do not teach, suggest or motivate association of growth factors with valved protheses or the association of biologically active molecules with a substrate using a biological adhesive. Therefore, the combination of the references does not render claims 6-8, 14, 15, 21-24, and 27-28 obvious.

Claims 6-8, 14, 15, 21-24, 27 and 28 are grouped together for purposes of this appeal. Appellants do not admit that there are no patentable differences amongst claims 6-8, 14, 15, 21-24, 27 and 28. Further, claims 15 and 21-24 are dependent from claim 14 and thus will stand and fall together with claim 14. Since claim 14 is patentable, claims 15, 21-24 are also in condition for allowance.

In view of the above, the references cited fail to or motivate one to arrive at the invention of claims 6-8, 14, 15, 21-24, 27 and 28. These claims are patentable under 35 U.S.C. §103(a) over the Bayne EP application and the Wadström patent as applied to claims 1-5, 9-11 and 29, and further in view of the Carpentier patent.

Conclusion

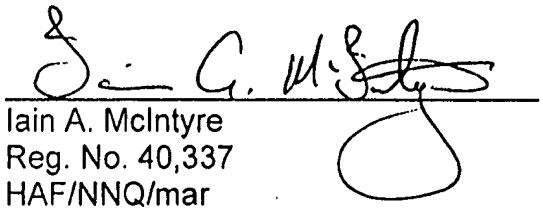
Appellants respectfully submit that claims 1-2, 4-11, 14-15, and 21-29 are not anticipated by the prior art cited and that no *prima facie* showing of obviousness has been established with respect to claims 1-2, 4-11, 14-15 and 21-29, the rejection of which are contested by Appellants. It is earnestly requested that the rejections be reversed, and that all pending claims 1-2, 4-11, 14-15 and 21-29 be allowed.

If a telephone conference would be helpful in resolving any issues concerning the communication, please contact Iain A. McIntyre at 952.253.4110

Respectfully submitted,

Altera Law Group, LLC

Date: May 23, 2003

By: 

Iain A. McIntyre
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APPENDIX 1
THE CLAIMS ON APPEAL (as finally amended)

1. (Previously Amended) A prosthesis for a human patient comprising allograft or xenograft tissue having a polypeptide growth factor associated therewith by a biologic adhesive, antibody-antigen associations, specific binding protein-receptor associations or enzyme substrate associations, said polypeptide growth factor being effective to stimulate the affiliation of viable cells with said tissue.

2. (Original) The prosthesis of claim 1 wherein said binding of said polypeptide growth factor to said tissue involves specific binding interactions.

3. (Cancelled).

4. (Original) The prosthesis of claim 1 wherein said binding of said polypeptide growth factor to said tissue involves a linker molecule.

5. (Original) The prosthesis of claim 1 wherein said tissue comprises crosslinked tissue.

6. (Original) The prosthesis of claim 1 wherein said tissue comprises uncrosslinked tissue.

7. (Original) The prosthesis of claim 1 wherein said tissue comprises a porcine heart valve.

8. (Original) The prosthesis of claim 1 wherein said tissue comprises bovine pericardial tissue.

9. (Original) The prosthesis of claim 1 wherein said polypeptide growth factor comprises vascular endothelial growth factor.

10. (Original) The prosthesis of claim 9 wherein said vascular endothelial growth factor comprises a protein selected from the group consisting of bVEGF164, bVEGF120, hVEGF165, hVEGF121, VEGF II, hVEGF80, VEGF-B, VEGF2, modified active forms thereof, and combinations thereof.

11. (Original) The prosthesis of claim 1 wherein said tissue comprises synthetic tissue.

12. (Cancelled).

13. (Cancelled)

14. (Previously Amended) A prosthetic heart valve comprising a substrate with associated VEGF, wherein said VEGF is associated with the substrate by direct attachment, a biologic adhesive, covalent bonding using crosslinking agents, antibody-antigen associations, specific binding protein-receptor associations or enzyme-substrate associations, the prosthesis having a valve structure, said polypeptide growth factors being effective to stimulate the affiliation of viable cells with said substrate.

15. (Previously Amended) The prosthetic heart valve of claim 14 wherein said prosthetic heart valve comprises a porcine or bovine heart valve.

16. (Cancelled).

17. (Cancelled).

18. (Cancelled).

19. (Cancelled)

20. (Cancelled).

21. (Previously Added) The prosthetic heart valve of claim 14 wherein the substrate comprises tissue.

22. (Previously Added) The prosthetic heart valve of claim 21 wherein said tissue comprises uncrosslinked tissue.

23. (Previously Added) The prosthetic heart valve of claim 21 wherein said tissue comprises crosslinked tissue.

24. (Previously Added) The prosthetic heart valve of claim 14 wherein the substrate comprises a synthetic polymer.

25. (Previously Added) A prosthesis comprising crosslinked tissue having an exogenous polypeptide growth factor associated therewith.

26. (Previously Added) The prosthesis of claim 25 wherein said polypeptide growth factor comprises vascular endothelial growth factor.

27. (Previously Added) The prosthesis of claim 25 wherein said crosslinked tissue comprises a crosslinked heart valve.

28. (Previously Added) The prosthesis of claim 25 wherein said crosslinking involves glutaraldehyde moieties.

29. (Previously Amended) A prosthesis for a human patient comprising allograft or xenograft tissue having a polypeptide growth factor associated therewith by a biologic adhesive, covalent bonding using crosslinking agents comprising reactive functional groups, antibody-antigen associations, specific binding protein-receptor

associations or enzyme substrate associations, said polypeptide growth factors being effective to stimulate the affiliation of viable cells with said tissue.

APPENDIX 2

OFFICE ACTIONS AND AMENDMENTS/RESPONSES

A. Non-final Office Action mailed March 30, 1999

B. Amendment filed April 23, 1999

C. Non-final Office Action mailed July 7, 1999

D. Amendment filed October 7, 1999

E. Letter to the Official Draftsperson, Petition to Accept Photographs with three sets of photographs filed December 2, 1999

F. Final Office Action mailed January 5, 2000

G. Amendment filed March 3, 2000

H. Advisory Action mailed March 28, 2000

I. Request for Continued Prosecution Application (CPA) filed April 4, 2000

J. Non-final Office Action mailed May 26, 2000

K. Amendment filed August 28, 2000

L. Final Office Action mailed November 30, 2000

M. Amendment filed January 29, 2001

N. Advisory Action mailed February 12. 2001

O. Request for Continued Examination (RCE) filed February 26, 2001

P. Non-final Office Action mailed May 24, 2001

Q. Amendment filed August 23, 2001

R. Final Office Action mailed November 29, 2001

S. Amendment filed January 29, 2002

T. Advisory Action mailed February 28, 2002

U. Request for Continued Examination (RCE) filed February 28, 2002

V. Non-final Office Action mailed May 10, 2002

W. Response filed August 19, 2002

X. Final Office Action mailed November 25, 2002

Y. Amendment filed January 27, 2003

Z. Advisory Action mailed February 7, 2003

2AA. Notice of Appeal filed February 25, 2003

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MATTER: 1610-53us01

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